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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,339	03/19/2004	Patricia Cruz-Perez	0001-00001CON1	8012

7590 08/14/2006

Patricia Cruz, Ph.D.
Harry Reid Center for Environmental Studies
4505 Maryland Parkway
Box 454009
Las Vegas, NV 89154-4009

EXAMINER	
WOOLWINE, SAMUEL C	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 08/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/804,339	CRUZ-PEREZ ET AL.	
	Examiner	Art Unit	
	Samuel Woolwine	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status

Claims 18-27 are pending in the application and were rejected in the Office action dated 2/8/2006. Any rejections not reiterated in the Office action below has been withdrawn as no longer applicable.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 18 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Haugland et al (1999).

With regard to claim 18, Haugland teaches a method comprising:

obtaining a primer set and probe that is specific for the fungal species Stachybotrys chartarum; See page 334, first sentence of *Results*: "The sequences and target sites of the forward (StacF4) and reverse (StacR5) PCR primers and TaqMan probe (StacP2) constructed for the detection of *S. Chartarum* rDNA sequences in this study are shown in Fig. 1." See also figure 1.

collecting the sample from the environment; See page 333, first sentence of *Collection, recovery and analysis of conidia from air samples*: "Air sampling was performed in rooms that had previously been occupied by infants diagnosed with PH from three homes in the Cleveland, Ohio area."

extracting the sample's DNA; See page 334, last sentence of first paragraph on the page: "Three additional 10µl aliquots of each recovered sample were mixed with *G. candidum* reference conidia and subjected to total genomic DNA extraction for subsequent analysis in the model 7700 as specified above."

obtaining DNA standards from a culture of Stachybotrys chartarum; See page 330, first sentence of second paragraph under *Fungal cultures, conidia stocks and genomic DNA extraction*: "Genomic DNAs were extracted from 20µl conidia suspensions using a glass bead milling and glass milk adsorption method."

determining the concentration of Stachybotrys chartarum spores in the DNA standards; See page 330, fourth sentence of first paragraph under *Fungal cultures, conidia stocks and genomic DNA extraction*: "Cell concentrations in these stock suspensions were determined by counting under a microscope at 400× magnification in a haemocytometer chamber, after which the suspensions were divided into ~200µl aliquots for storage at -80°C."

amplifying by polymerase chain reaction each of the DNA standards and the collected sample's DNA using the obtained primer set and probe; See page 332, *PCR amplification and TaqMan analysis in the model 7700*, entire section.

and comparing amplification plots obtained by polymerase chain reaction of each of the DNA standards and the collected sample's DNA to obtain an indication of the presence of the fungus Stachybotrys chartarum in the collected sample and a concentration of the fungus Stachybotrys chartarum in the collected sample. See page 332, last paragraph of *Quantification of S. chartarum conidia using the comparative* C_T

method: "Each series of DNA extracts was also analysed using only *S. chartarum* target sequence assay results. In these calculations, calibrator [i.e. standard] sample C_T values were subtracted directly from corresponding test sample C_T values to obtain $\Delta C_{T,STAC}$ values. These values were used in place of $\Delta\Delta C_T$ values to determine the ratio of target sequences in the test and calibrator samples and to quantify *S. chartarum* conidia in the test samples as described above."

With regard to claim 21, *wherein the concentration of Stachybotrys chartarum spores in the DNA standards is determined via direct total count of the Stachybotrys chartarum spores in the DNA standards*, Haugland teaches on page 330, fourth sentence of first paragraph under *Fungal cultures, conidia stocks and genomic DNA extraction*: "Cell concentrations in these stock suspensions were determined by counting under a microscope at 400× magnification in a haemocytometer chamber, after which the suspensions were divided into ~200µl aliquots for storage at -80°C."

Claim Rejections - 35 USC § 102 –Response to arguments

Applicant's arguments filed 6/13/2006 have been fully considered but they are not persuasive.

Applicant's traversal of the rejection begins on page 9 of the response, asserting that Haugland does not disclose or suggest "obtaining DNA standards from a culture of Stachybotrys chartarum", "determining the concentration of Stachybotrys chartarum spores in the DNA standards", "amplifying by polymerase chain reaction each of the DNA standards and the collected sample's DNA using the obtained primer set and probe" and "comparing amplifcation plots obtained by polymerase chain reaction of

each of the DNA standards and the collected sample's DNA to obtain an indication of the presence of the fungus Stachybotrys chartarum in the collected sample and a concentration of the fungus Stachybotrys chartarum in the collected sample," as recited in claim 18. This argument is not persuasive, as Haugland discloses each of these limitations as distinctly indicated in the rejection above.

Applicant argues in the last paragraph of page 9, and continuing throughout pages 10 and 11 of the response, that Haugland determines the concentration of spores in the standards by microscopic counting, whereas Applicant determines the concentration by electronic particle counting. In addition, Applicant characterizes Haugland's method as "relative quantitation" rather than the "absolute quantitation" of Applicant's method. This argument is not persuasive. As a first point, the means by which the concentration of spores in the DNA standards is not found in the claim (and even if the claim were amended to include "electronic particle counting", the claim would still be rejectable under 35 USC § 103 in view the microscopic analysis of Haugland). Secondly, Applicant's assertion that the quantitation of Haugland's method is "relative" while the quantitation of the claimed methods is "absolute" is not persuasive because: (a) there is no evidence to support this assertion, and (b) this is not a distinction supported by the claim limitations. There is no patentable distinction between the "quantitation" of the claimed method and the "quantitation" of Haugland.

In the final paragraph of page 11, continuing on page 12 of the response, Applicant argues that Haugland's method is not based on "direct comparison to S. chartarum standards". Haugland *does* directly compare the amplification profiles of test

and standard using two different methodologies. In the first method, an internal reference (Geotrichum candidum) is used to normalize the C_T values of test and standard [i.e. calibrator] samples. Then "[c]alibrator sample ΔC_T values are then subtracted from ΔC_T values of the test samples to obtain $\Delta\Delta C_T$ values" (last sentence, column 1, page 332). In the second method, "calibrator [i.e. standard] sample C_T values were subtracted directly from corresponding test sample C_T values to obtain $\Delta C_{T,STAC}$ values" (page 332, last paragraph of *Quantification of S. chartarum conidia using the comparative C_T method*).

Thus, Haugland teaches each limitation found in the methods of claims 18 and 21 and the rejection of these claims is proper.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 19-20 and 22-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haugland et al (1999) in view of Buck et al (1999) and GenBank ® GI: 3420911.

With regard to claims 19-20 and 22-27, Haugland teaches a method comprising:

obtaining a primer set and probe that is specific for the fungal species Stachybotrys chartarum; See page 334, first sentence of *Results*: "The sequences and target sites of the forward (StacF4) and reverse (StacR5) PCR primers and TaqMan probe (StacP2) constructed for the detection of *S. Chartarum* rDNA sequences in this study are shown in Fig. 1." See also figure 1.

collecting the sample from the environment; See page 333, first sentence of *Collection, recovery and analysis of conidia from air samples*: "Air sampling was performed in rooms that had previously been occupied by infants diagnosed with PH from three homes in the Cleveland, Ohio area."

extracting the sample's DNA; See page 334, last sentence of first paragraph on the page: "Three additional 10µl aliquots of each recovered sample were mixed with *G. candidum* reference conidia and subjected to total genomic DNA extraction for subsequent analysis in the model 7700 as specified above."

obtaining DNA standards from a culture of Stachybotrys chartarum; See page 330, first sentence of second paragraph under *Fungal cultures, conidia stocks and genomic DNA extraction*: "Genomic DNAs were extracted from 20µl conidia suspensions using a glass bead milling and glass milk adsorption method."

determining the concentration of Stachybotrys chartarum spores in the DNA standards; See page 330, fourth sentence of first paragraph under *Fungal cultures, conidia stocks and genomic DNA extraction*: "Cell concentrations in these stock suspensions were determined by counting under a microscope at 400× magnification in a haemocytometer chamber, after which the suspensions were divided into ~200µl aliquots for storage at -80°C."

amplifying by polymerase chain reaction each of the DNA standards and the collected sample's DNA using the obtained primer set and probe; See page 332, *PCR amplification and TaqMan analysis in the model 7700*, entire section.

and comparing amplification plots obtained by polymerase chain reaction of each of the DNA standards and the collected sample's DNA to obtain an indication of the presence of the fungus Stachybotrys chartarum in the collected sample and a concentration of the fungus Stachybotrys chartarum in the collected sample. See page 332, last paragraph of *Quantification of S. chartarum conidia using the comparative* C_T

method: "Each series of DNA extracts was also analysed using only *S. chartarum* target sequence assay results. In these calculations, calibrator [i.e. standard] sample C_T values were subtracted directly from corresponding test sample C_T values to obtain $\Delta C_{T,STAC}$ values. These values were used in place of $\Delta\Delta C_T$ values to determine the ratio of target sequences in the test and calibrator samples and to quantify *S. chartarum* conidia in the test samples as described above."

Further, with regard to the limitation *wherein the concentration of Stachybotrys chartarum spores in the DNA standards is determined via direct total count of the Stachybotrys chartarum spores in the DNA standards*, Haugland teaches on page 330, fourth sentence of first paragraph under *Fungal cultures, conidia stocks and genomic DNA extraction*: "Cell concentrations in these stock suspensions were determined by counting under a microscope at 400× magnification in a haemocytometer chamber, after which the suspensions were divided into ~200µl aliquots for storage at -80°C."

The only limitations of claims 19-20 and 22-27 not taught by Haugland are the specific primers/probes (SEQ ID NOS 1-5) used for the quantification of *Stachybotrys chartarum*. SEQ ID NOS 1-5 were all known sequences of the 18S ribosomal RNA gene of *Stachybotrys chartarum* at the time the invention of the instant application was made as shown by GenBank ® GI: 3420911.

SEQ ID NO 1

>gi|3420911|gb|AF081469.1|AF081469 Stachybotrys chartarum strain UAMH 7900 18S ribosomal RNA gene, partial sequence; internal transcribed spacer 1, 5.8S ribosomal RNA gene and internal transcribed spacer 2, complete sequence; and 28S ribosomal RNA gene, partial sequence
Length=936

```
 Score = 34.2 bits (17),  Expect = 2e-05
 Identities = 17/17 (100%), Gaps = 0/17 (0%)
 Strand=Plus/Plus

Query  1    GTTGCTTCGGCGGGAAC  17
            ||||||||||||||||
Sbjct  405  GTTGCTTCGGCGGGAAC  421
```

SEQ ID NO 2

>gi|3420911|gb|AF081469.1|AF081469 Stachybotrys chartarum strain UAMH 7900 18S ribosomal RNA gene, partial sequence; internal transcribed spacer 1, 5.8S ribosomal RNA gene and internal transcribed spacer 2, complete sequence; and 28S ribosomal RNA gene, partial sequence
Length=936

```
 Score = 40.1 bits (20),  Expect = 5e-07
 Identities = 20/20 (100%), Gaps = 0/20 (0%)
 Strand=Plus/Minus

Query  1    TTTGCGTTTGCCACTCAGAG  20
            ||||||||||||||||||||
Sbjct  511  TTTGCGTTTGCCACTCAGAG  492
```

SEQ ID NO 3

>gi|3420911|gb|AF081469.1|AF081469 Stachybotrys chartarum strain UAMH 7900 18S ribosomal RNA gene, partial sequence; internal transcribed spacer 1, 5.8S ribosomal RNA gene and internal transcribed spacer 2, complete sequence; and 28S ribosomal RNA gene, partial sequence
Length=936

```
 Score = 38.2 bits (19),  Expect = 2e-06
 Identities = 19/19 (100%), Gaps = 0/19 (0%)
 Strand=Plus/Plus

Query  1    ACCTATCGTTGCTTCGGCG  19
            |||||||||||||||||||
Sbjct  398  ACCTATCGTTGCTTCGGCG  416
```

SEQ ID NO 4

```
>gi|3420911|gb|AF081469.1|AF081469  Stachybotrys chartarum strain UAMH 7900 18S ribosomal RNA gene,
partial sequence; internal transcribed spacer 1, 5.8S ribosomal
RNA gene and internal transcribed spacer 2, complete
sequence; and 28S ribosomal RNA gene, partial sequence
Length=936

 Score = 46.1 bits (23),  Expect = 1e-08
 Identities = 23/23 (100%), Gaps = 0/23 (0%)
 Strand=Plus/Minus

Query  1    GCGTTTGCCACTCAGAGAATACT  23
            |||||||||||||||||||||||
Sbjct  508  GCGTTTGCCACTCAGAGAATACT  486
```

SEQ ID NO 5

```
>gi|3420911|gb|AF081469.1|AF081469  Stachybotrys chartarum strain UAMH 7900 18S ribosomal RNA gene,
partial sequence; internal transcribed spacer 1, 5.8S ribosomal
RNA gene and internal transcribed spacer 2, complete
sequence; and 28S ribosomal RNA gene, partial sequence
Length=936

 Score = 36.2 bits (18),  Expect = 7e-06
 Identities = 18/18 (100%), Gaps = 0/18 (0%)
 Strand=Plus/Plus

Query  1    CTGCGCCCGGATCCAGGC  18
            ||||||||||||||||||
Sbjct  433  CTGCGCCCGGATCCAGGC  450
```

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

> "Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties"

Since the claimed primers/probes simply represent functional homologues of the primers/probes taught by Haugland, the claimed primers/probes are *prima facie* obvious over Haugland's primers/probes in the absence of secondary considerations.

Buck expressly provides evidence of the equivalence of primers. Specifically,

Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

Since the rejection is based on the conclusion that it would have been obvious to one of ordinary skill in the art to make and use the primers and probes of the claimed methods, being functionally equivalent to those used by Haugland, the limitation "wherein the forward primer, reverse primer and probe do not cross-react with other fungal species when used in combination in polymerase chain reaction" would necessarily have been met.

Claim Rejections - 35 USC § 103 –Response to arguments

Applicant's arguments filed 6/13/2006 have been fully considered but they are not persuasive.

Applicant argues on page 13 of the response that a *prima facie* case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities, and cites *In re Payne*. Although the rejection above does not cite *In re Payne*, the rejection is in fact consistent with *Payne*, since the primers of Haugland and the primers of the claimed methods have similar utilities (i.e. amplification and detection of S. chartarum nucleic acid sequences). In addition, the primers have "very close structural similarities" in that both comprise an identical sugar-phosphate backbone which makes up a significant portion of the molecule.

Applicant argues that "the primers disclosed in HAUGLAND do not establish a *prima facie* case of obviousness by themselves" (last sentence on page 13 of the response). This is not persuasive because the rejection is not based on Haugland alone, but on the disclosed method of Haugland and the known sequences from which the primers of the claimed methods are derived. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues of pages 14 and 15 that *In re Deuel*, cited in the rejection above, does not support a *prima facie* case of obviousness because this case "does not

support the proposition alleged in the Office Action that chemical compounds that may perform similar functions are *prima facie* obvious over one another". This is not persuasive because the rejection is based on Haugland et al (1999) in view of Buck et al (1999) and GenBank ® GI: 3420911. *In re Deuel* is not the basis for the rejection, but merely demonstrates the courts have recognized the obviousness to one of ordinary skill in the art to take a prior art compound and modify it: "[s]tructural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds".

Here, the known prior art sequence disclosed in GenBank ® GI: 3420911 renders the primers of the claimed methods obvious, because the structure of the latter is completely found within the former. In view of Buck et al, who show that different primers can be designed from different parts of a given known sequence and used successfully to generate sequencing data, one of ordinary skill in the art would have been motivated to produce and use the methods of the claimed primers based on the known sequence of GenBank ® GI: 3420911, since these primers represent equivalents of the primers used by Haugland, and as stated in *Deuel*, "a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties".

MPEP 2144.06 provides for the obviousness of substituting equivalents known for the same purpose. Here, the primers of the claimed methods clearly would have

represented equivalents of Haugland's primers to one of ordinary skill in the art for the purpose of practicing Haugland's method.

Applicant argues on page 15 of the response that "Buck does not demonstrate that there is a reasonable expectation of success". This argument is not persuasive as Buck clearly shows that one of ordinary skill in the art would have had *more* than a reasonable expectation of success in designing a primer from a known sequence and using it in the manner in which a primer is used in the method of Haugland and in the claimed methods, i.e. hybridizing to a target sequence and being extended by a polymerase.

The declaration submitted by Dr. Stetzenbach on behalf of Applicants has been considered but the arguments therein are also not considered persuasive. As a minor point, Dr. Stetzenbach is an acquaintance and former mentor of Dr. Cruz-Perez. Thus while having stated Dr. Stetzenbach has no financial interest in the instant application, her testimony is not as objective as would be the testimony of an expert with no relationship to the Applicants.

The testimony beginning at the bottom of page 2 and continuing at the top of page 3 of the declaration asserts that , while species-specific primers and probes can theoretically be derived from any DNA sequence, a unique region in the target genome needs to be located first. The testimony then states that extensive research would have to be conducted to find primers that will not cross-react with other organisms. This testimony is not persuasive. Homology searches in sequence databases was routinely used in the art at the time the invention of the instant application was made (for

example, the commonly used BLAST algorithm was introduced in 1990). This analysis could have been performed rather easily over the internet. For example, the sequence alignments depicted in the rejection above took less than 30 minutes for the examiner to produce using the BLAST algorithm on the National Center for Biotechnology Information (NCBI) web site (http://www.ncbi.nlm.nih.gov/). The experimentation needed to determine whether a particular primer pair/probe set cross-reacted with other fungal species could have performed in a single PCR experiment in less than one day (assuming one already had the primers and probes synthesized and genomic DNA from other fungal species prepared). This would not have been considered "extensive" research by one of ordinary skill in the art in 2001.

The testimony continues on page 4, stating that while the criteria for selecting sequencing primers are flexible as demonstrated by Buck, the selection of optimal primers for PCR follows very stringent criteria and is not predictable to troubleshoot. This is not persuasive because in both PCR and sequencing reactions, the function of the primer is to hybridize to a target and be extended by a polymerase. One of ordinary skill in the art would have had a reasonable expectation of success in designing primers and probes based on the known sequence of GenBank ® GI: 3420911, for the purpose of detecting S. chartarum. As discussed in the preceding paragraph, there were readily available tools prior to 2001 for comparing sequences to find regions unique for a target of interest, and testing primers and probes for specificity would not have involved "extensive" research.

Thus based in view of Haugland, who teaches the methods claimed but for the particular primers and probes used, and in view of GenBank ® GI: 3420911, which discloses a known S. chartarum sequence in which can be found the sequences of the primers and probes of the claimed methods, and in view of Buck, who demonstrates that one of skill in the art would have had a reasonable expectation that any primer designed from a known sequence would function, thus proving the functional equivalents of such primers, the rejections of claims 19-20 and 22-27 is proper.

Double Patenting

The nonstatutory double patenting rejection is withdrawn in view of the terminal disclaimer filed 6/13/2006.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Woolwine whose telephone number is (571) 272-1144. The examiner can normally be reached on Mon-Fri 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

scw

JEFFREY FREDMAN
PRIMARY EXAMINER
9/1/06